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10/812,088	03/30/2004	Sunil Kochhar	88265-6699	3008

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EXAMINER

HARLE, JENNIFER I

ART UNIT	PAPER NUMBER
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1654

DATE MAILED: 12/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/812,088	KOCHHAR ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Jennifer I. Harle	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
  - If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
  - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
  - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 15 October 2004.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-20 is/are pending in the application.
- 4a) Of the above claim(s) 2-4, 6, 7, 10-16, 18 and 19 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1, 5, 8, 9, 17 and 20 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)  | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date <u>03/30/04</u> . | 6) <input type="checkbox"/> Other: _____  |

## **DETAILED ACTION**

### ***Election/Restrictions***

1. Applicant's election with traverse of Group I, the composition Arg-Phe, claims (1-5 and 8-15 in part) in the reply filed on October 15, 2004 is acknowledged. The traversal is on the ground(s) that the inventions are species variations and not independent and distinct and that the search imposes no additional burden. First, the examiner would like to correct one typographical error, the claims should have read 8-14, as the grouping was toward the composition and there was a separate grouping already containing claim 15 with the food/cosmetic/pharmaceutical product and thus, claim 15 belongs with that grouping. This is not found persuasive because the examiner noted that the Groups 1-22 and 23-44 were related as subcombination usable together and not independent inventions. Applicants arguments are directed to "independent and distinct inventions" not the subcombination arguments of the examiner, which clearly showed that the inventions each of inventions 1-22 have separate utilities as aromas and as flavorings to be utilized in Groups 23-44 different products – foods, pharmaceuticals and cosmetics. The classification is irrelevant to whether or not the groups have separate utilities.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 2-4 (do not contain the composition Arg-Phe), 6-7, 9-16 (note that claims 10-14 do not contain the composition Arg-Phe), and 18-19 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on October 15, 2004.

Thus, claims 1, 5, 8-9, 17 and 20 are not withdrawn from consideration.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1, 5, 8-9, 17 and 20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicants claim “a flavor active compound obtainable by subjecting one or more peptides selected from the group consisting of ... to a Maillard reaction with reducing sugars under conditions sufficient to form the flavor active compound.” However, the Specification lacks adequate written description such that one of ordinary skill in the art would immediately envisage the product claimed from the disclosed process, i.e. any and all compounds/flavors - these would consist of a vast and nuanced set of “flavors/aromas” ranging from bitter to sweet/vegetable to flower to meat to nut/vanilla to chocolate to coffee, etc.. The Specification states the specific peptides are obtainable from cocoa beans and give rise to particular and distinct savor when subject to a Maillard reaction with reducing sugars for the preparation of a chocolate flavor, specifically a cocoa and caramel flavor, a floral or more specifically, a bonbon flavor, bready flavor, or a roasted or meaty flavor. Specification, pg 1, lines 9-13. The Specification further discloses that the size of the peptides and their amino acid contents/sequence play an important role in flavor development and that thermal reaction of a mixture of fructose/glucose and hydrophobic amino acids under low water activity medium, e.g.

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glycerol or propylene glycol, etc. give rise to a chocolate-like **aroma**. Specification, pp. 1-2.

The Specification adds that using this type of react **flavor** as a base and combining it with certain top notes, most prominent, vanilla, chocolate-like flavor concentrates *could be* produced.

Specification, pg. 2. The Specification utilizes flavor and aroma interchangeable and also utilizes the word savor, which can mean the property of a thing which affects the organs of taste or smell and states that the compounds obtained from the Maillard reaction or generically the peptides listed, may be used for the preparation of any product, wherein an aroma provided by the subjective compounds is desired. Specification, pp. 2-3. The Specification then shows how to identify the di-peptides from cocoa Figs. 1-3 and pp. 4-7. Once again, the Specification speaks of the “flavors” in terms of aroma to determine the potential of the dipeptides. See, pg. 7, line 31 – pg. 10, line 2. The Specification then discloses a Peptide Model Reaction, similar to a Maillard Reaction, with a specific sugar, reactant, and pH range along with Sensory Profiling. Specification, pp. 11-12. However, nowhere, is there any demonstration of any tasting profile, specific compounds obtained, or any specific tastes that are obtained, or a specific reaction performed on a specific di-peptide to obtain a specific compound that would provide a specific taste not an aroma. Nor are any specific compounds themselves provided from the outcome of the reaction itself. In the claimed flavor active compound, Applicant claims 24 di-peptides, however, Applicants only recite that the flavor active compounds are obtainable not obtained by subjecting one or more di-peptide to a Maillard reaction with reducing sugars under conditions “sufficient” to form the flavor active compound. While the specification provides limited guidance with respect to the Maillard reaction, the mechanism of the Maillard reaction is very complicated and strongly affected by factors, which influence the different chemical reactions

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involved, i.e. temperature and duration of heating, pH and presence of weak acids and bases, water content, type of reactant, amino acid and sugar ratio and oxygen content. See Davies, et al. The Maillard Reaction application to Confectionery Products, Confectionary Science, 1997, pp. 1-33, [http://courses.che.umn.edu/00scn8334\\_1f/FSCN8334\\_Reading.html](http://courses.che.umn.edu/00scn8334_1f/FSCN8334_Reading.html), last updated September 26, 2000, particularly pp. 3 and 13. While the Specification provides limited parameters, i.e. one of the claimed sugars, some information on heating but not all, the length of time the pre-heating occurs, the water content, amount of propylene glycol, how long the mixture was heated – length of time is important and we know it was heated up to 60 minutes but it could have been anywhere from 1-60. Additionally, the rate of reaction depends on the rate at which the sugar ring opens to the reducible, open-chained form and this increases with increasing pH, i.e. pentoses react more rapidly than hexoses and relative rate of browning also depends on the extent to which the reaction mixture is buffered, i.e. in unbuffered media, the rate of browning of fructose with amino acids is greater than that of glucoses and for hexoses the order of reactivity is D-galactose>D-mannose>D-glucose and reducing disaccharides are considerably less reactive than their corresponding monomers. *Id.* at 13-14. Moreover the Maillard reaction, also is dependent upon the type of amines, i.e. basic amino acids are more reactive than neutral or acidic amino acids, which led one author to suggest a classification of amino acids into three groups depending on the extent of browning when reacted with glucose at different, pH, and 121 degrees C for 10 minutes, while other results show that comparisons can only be used if the same pH and buffering conditions exist, i.e. the effect of pH is especially significant due to the different pK<sub>a</sub> values of the amino acids. *Id.* at 15. Thus, it has been determined that at least the amount of browning is not, *per se*, proportional to the conversion of amino acid or peptides, as

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the degree of browning depends on the type of melanoidin formed during the Maillard reaction and that small peptides are more reactive than corresponding peptides. *Id.* at 15-16. The Specification fails to provide any guidance with respect to the differences between the peptides and their different rate of reaction for the various sugars, i.e. only one sugar, fructose, is disclosed, or the different types of amines that need to be taken into account because of the different types of amino acids in the di-peptides. Additionally, the Specification lacks guidance on the reactant ratio, i.e. the extent of browning seems to vary according to the sugar/amine ratio, but the extent that this will occur is unknown. *Id.* at 16-17. Further, different flavors are formed at different temperatures, thus the length of heating is also important as the formation melanoidins usual occurs at a rate which increases in proportion to the square of the reaction time at any given temperature and different flavors are formed depending on the extent of the reaction, however, most temperature studies have only considered color development and, thus, there is only a little information on the effect of temperature on the effect on flavor formed during browning, very little data exists on rate or activation energies, thus, at any given temperature-time combination, a unique aroma profile is produced. *Id.* at 19-21. The specification lacks guidance as to the temperature-time combination, and only states minimally that the predefine mixture was added to preheated propylene glycol and does not specify any length of time and that the reaction mixture was heated up to 60 minutes, which could be anywhere from 1 up to 60 minute and does not specify any temperature for the heating. Specification – Peptide Model Reaction – Pg. 11. Thus, there it is uncertain what if any flavor compound is obtained. Davies discloses that for the first stage of the Maillard reaction to occur, water is essential and thus, the rate of the reaction is dependent on the amount of free water

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available as related to water activity and that the temperature-moisture profile will control the rate of flavor and color development. Davies, pp. 22-24. However, the specification lacks guidance with respect to the amount of water to be used and only provides limited guidance with respect to the fact that a reactant is used, i.e. propylene glycol. Davies also discloses that the pH has a significant effect on the Maillard reaction and that in general the rate and extent of browning increases with increasing pH, with an optimum above pH 7, leading to a change in the mechanism of the reaction and, hence to the formation of different and volatile and colored products – noting that the pH dependence of the initial step of the reaction can be related to the amount of the unprotonated amine present, the rate of the Maillard reaction is lower at a pH lower than the pKa of the reactive amino group, that one should also note that as temperature increases the pH decreases, and that the rate of the reaction is also dependent on the concentration of acyclic sugar present as noted earlier. The Specification lacks guidance as to the pH with different sugars, although it does utilize the optimum range in the model, it makes no discussion of whether this range would always be appropriate taking all of the other factors into account.

Thus, while the Specification sets forth recitations of “flavors” obtainable by subjecting di-peptides to a Maillard reaction with reducing sugars under conditions sufficient to form the flavor active compound, the Peptide Model Reaction fails to provide an adequate description of the full scope of the “flavors” encompassed by Applicants claims, including the claim limited to Arg-Phe, because the parameters of the reaction determine the scope of the “flavors,” if any, the only flavor provided is chocolate, no compound is set forth, and it is not routine to one of skill in the art to obtain a flavor/aroma/compound, as shown by Davies. There are no known structural



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characteristics in common between any of the flavor active compounds, only an aroma and even that according to Davies may or may not remain depending upon a plethora of factors that are lack guidance.

Applicant appears to have created a specification based upon functional characteristics, the compounds making up a library that are obtainable through the Maillard reaction and produce a "flavor." The compounds appear to be described by what they do rather than what they are, i.e. flavor active compounds obtainable by subjecting di-peptides to a reaction, noting that the di-peptides do not even have to be subjected to that reaction. It is also noted that not one of the peptides is shown to have a flavor from the reaction, there are only aromas associated with the sensory test.

4. Claims 1, 5, 8-9, 17 and 20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

A number of factors would prevent one of ordinary skill in the art from practicing the invention without undue experimentation.

The specification fails to give any guidance as to the breadth of the claims. The claims involve "a flavor active compound obtainable by subjecting one or more peptides to a Maillard reaction with reducing sugars under conditions sufficient to form the flavor active compound." The breadth of the claims is open-ended regarding the structure, as it is only described as a compound obtainable by subjecting a di-peptide to a reaction, i.e. could be subjected to but does not have to be. Moreover, even if it is subjected to the reaction, there is not structure that is

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ascertainable from the reaction, as it depends upon multiple factors and products within the reaction that are not set forth. As set forth above and explained in Davies, the plethora of reaction conditions, can result in a plethora of compounds for one di-peptide, i.e. the sugar, the temperature, the pH, the time of each step and its relation to the other reactants, the reactant, etc.

The nature of the invention is flavor active compounds obtainable by subjecting one or more di-peptides to a Maillard reaction with reducing sugars under conditions sufficient to form the flavor active compound. Applicants vacillate between aroma in the Specification and actual taste. See arguments above.

The state of the prior art is such that according to Applicants' own specification little is known of the short-chain peptides that are present in the cocoa peptide pool. Specification, pg. 1, lines 34-35. Applicants' own teachings of thermal reactions with hydrophobic amino acids under low water activity medium, while giving rise to chocolate-like aromas are complex in nature. Specification, pg. 2, lines 1-16. Moreover, as set forth above Davies discloses that the Maillard reaction, while well-known, is extremely complex and just beginning to become predictable with model system containing one sugar and amino acid, the chemistry of these compounds is not well-known, their formation mechanism remains obscure and can result in undesirable products. Davies, pp. 5-6, 9-10, and 30. Thus, the level of one of ordinary skill in the art would be high, as he would have to be able to take into account all of the factors of the Maillard reaction and balance them against one another and have the ability to differentiate the aroma/taste desired.

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The level of predictability in the art is very low as set forth above. There are no model systems above one sugar and one amino acid and the variables are numerous and interdependent. See Davies discussion above under written description, i.e. temperature, pH, time, etc.

The Specification fails to give adequate direction and guidance as to the means of utilizing a Maillard reaction to obtain a flavor active compound. While the Specification does set forth a Peptide Model Reaction, it is rife with omissions and has only one example of a sugar and reactant. These omissions and the problems with only one sugar and reactant are discussed above under written description and result in the claimed invention being devoid of structural and or functional constraints regarding the compounds encompassed by the claimed "flavor active compounds."

The working examples directed to the Peptide Model Reaction and Sensory Profiling from that Model Reaction is clearly not commensurate in scope to the claimed invention, which is drawn to all flavor active compounds obtainable by subjecting one or more peptides selected from the group consisting of 24 di-peptides to a Maillard reaction with reducing sugars under condition sufficient to form the flavor active compound, when only one sugar is set forth, only one reactant, no parameters on time for preheating/mixing with the reactant, an up to limitation on the second heating, no guidance on the amount of water, no other reactants, the only one pH range, all of which are discussed above and give different flavor active compounds. Moreover, it is unclear how many example were tested, but it appears that only 6 were tested for aroma because it states that a maximum of 6 reaction samples was evaluated by sniffing at any given time. No real data is supplied other than for the six that were attributed a good chocolate aroma. Moreover, the aroma is only to chocolate not to all of the different possible aromas/flavors, i.e.

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the different fruits, vegetables, flowers, meats, bread, etc. Nor were they directed to the vast variety of chocolate aromas, i.e. bittersweet, vanilla, dark, coffee, etc. No examples of taste were provided.

Thus, the Specification provides insufficient disclosure to support or enable a flavor active compound obtainable by subjecting one or more of the 24 di-peptides or even just the one di-peptide Arg-Phe or a process for preparing a flavor, which comprises subjecting one or more of the 24 or even just the one di-peptide Arg-Phe to a Maillard reaction with reducing sugars under conditions sufficient to form the flavor for the reasons set forth above.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

5. Claims 1, 5, 8-9, 17 and 20 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term flavor renders the claim indefinite because it is unclear whether it is meant to be a taste, an aroma, a combination of both, or situational, i.e. either/or.

The phrase “flavor active compound” render the claim indefinite because it is unclear what a flavor active compound is, the structure is unknown, what constitutes a flavor active compound is unknown – is it a compound that has an aroma or a taste or both or sometimes one or the other or both, the Specification varies on its usage.

The term “obtainable” renders the claim indefinite because it is unclear whether or not the peptides have to be subjected to the Maillard reaction, as obtainable implies only that it might be done by that method but not that it is obtained by subjecting something to that reaction, i.e.

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the claims do not require the compound to be produced by the claimed product by process. It is suggested that Applicant amend the claim to recite, "obtained".

The term subjecting renders the claim indefinite because it is unclear what Applicant intends to encompass/mean by subjecting, as it is not an art recognized term in relation to a reaction. It is suggested that Applicants amend the claim to recite, "reacting".

The phrase "with a Maillard rereaction with reducing sugars" renders the claim indefinite because it is unclear when the sugars participate in the reaction, i.e. are they reacted with the peptides or at a later phase. It is suggested that the claim be amended to state that "and a reducing sugar to a Maillard reaction".

The phrase "under conditions sufficient to form the flavor active compound" is vague and indefinite" because the reaction itself is unpredictable it is unknown what conditions would be sufficient (see arguments above), also it lack metes and bounds because it is unclear what conditions are necessary in order to carry out the claimed process.

### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 1, 5, and 17 are rejected under 35 U.S.C. 102(b) as being anticipated by Otagiri, et al., Studies on a Model of Bitter Peptide Including Arginine, Proline, and Phenylalanine Residue. I. Bitter Taste of Di- and Tripeptides and Bitterness Increase of the Model Peptides by Extension of the Peptide Chain, Agric. Biol. Chem., 1985, Vol. 49, Iss. 4, pp. 1019-1026.

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Otagiri discloses a flavor active compound obtained from Arg-Phe, as the claim language merely states that the flavor active compound is "obtainable by" the subsection of the di-peptide to a Maillard reaction, it is not required that the di-peptide actually ever undergo the Maillard reaction to be a flavor active compound, see the 112 2<sup>nd</sup> paragraph rejection above, thus, all of the limitations are met, as the reference discloses that Arg-Phe was synthesized and became a bitter tasting compound. See pages 1019, 1021-1022 and 1025 specifically.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

7. Claims 1, 5, 8-9, 17 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Otagiri, et al., Studies on a Model of Bitter Peptide Including Arginine, Proline, and Phenylalanine Residue. I. Bitter Taste of Di- and Tripeptides and Bitterness Increase of the Model Peptides by Extension of the Peptide Chain, Agric. Biol. Chem., 1985, Vol. 49, Iss. 4, pp. 1019-1026 in view of Girsh (US 5,753,296).

As per 1, 5, 8, and 9, Otagiri discloses the di-peptide, Arg-Phe, and discloses that it has a bitter taste. See pages 1019, 1021-1022 and 1025 specifically. However, Otagiri does not disclose that the flavor active compound is obtained by subjecting Arg-Phe to the Maillard reaction with reducing sugars. Girsh discloses that is desirable to react cocoa powder protein (bitter protein) with lactose, i.e. a reducing sugar in the Maillard reaction in order to soften/sweeten the taste. Col. 11, lines 32-41. Thus, it would have been obvious to one of

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ordinary skill in the art at the time of the invention to have utilized the Maillard reaction with the bitter di-peptide of Otagiri and a reducing sugar to soften the bitter compound, i.e. making it more palatable.

As per claims 17 and 20, Otagiri and Girsh disclose as set forth above. Neither Otagiri nor Girsh disclose that the reducing sugar is fructose. However, fructose is the sugar that naturally occurs in fruits and would routinely or inherently be present in the confectionary/flavoring components, as conventional. Thus, it would have been obvious to one of ordinary skill in the art at the time of the invention to have utilized fructose in the place of lactose in the Maillard reaction as taught in Girsch with the peptide of Otagiri.

Claims 1, 5, 8-9, 17 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Otagiri, et al., Studies on a Model of Bitter Peptide Including Arginine, Proline, and Phenylalanine Residue. I. Bitter Taste of Di- and Tripeptides and Bitterness Increase of the Model Peptides by Extension of the Peptide Chain, Agric. Biol. Chem., 1985, Vol. 49, Iss. 4, pp. 1019-1026 in view of Yu-Chiang Oh, Flavor Chemistry of the Maillard Reaction of Dipeptides, Rutgers The State University of New Jersey – New Brunswick, 1992, pp. 1-154.

As per 1, 5, 8-9, 17 and 20, Otagiri discloses that the di-peptide, Arg-Phe, has a bitter taste. See pages 1019, 1021-1022 and 1025 specifically. However, Otagiri does not disclose that the flavor active compound is obtained by subjecting Arg-Phe to the Maillard reaction with reducing sugars, specifically fructose. Oh discloses that the contribution of dipeptides in the generation of balance food aroma can not be neglected, that it is known that many foods contained a variety of peptides, which play an important role in the contribution to the intrinsic property of a particular food aroma and that when Mohr, et al. conducted an experiment by pyrolyzing a mixture of

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peptides plus amino acids with fructoses, they found the aroma produced was much closer to that of roasted cocoa beans than when peptides or amino acids alone were pyrolyzed with fructose.

See, pg. 40. Additionally, Oh discloses that dipeptides/tripeptides are produced by thermal degradation during roasting, particularly dikeopiperazines (DKPs), which are known to give a bitter flavor in cocoa bean and sake. See, pp. 43 and 45. Oh further discloses that Rizzi observed that certain peptides, when reacted with fructose produced relatively more pyrazines than respective amino acid mixtures, i.e. the Maillard reaction of fructose with the peptides apparently facilitated peptide hydrolysis and formation of Strecker aldehydes. See, pg. 45.

Thus, it would have been obvious to one of ordinary skill in the art to subject the di-peptide, Arg-Phe, of Otagiri, to/in the Maillard reaction with the reducing sugar fructose to obtain more pyrazines, i.e. aroma/flavor compounds.

### ***Conclusion***

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Nosho, et al. Studies on a Model of Bitter Peptides including Arginine, Proline, and Phenylalanine Residues, Peptide Chemistry, 1984, pp. 323-328, discloses that Arg-Phe has a bitter flavor.

Kouge, et al., Relationship between Bitterness and Chemical Structure of Cyclic Dipeptides, Peptide Chemistry, 1978, pp. 105-108, discloses that Arg-Phe has a bitter flavor.

Keil, et al., Identification of the Bitter Principle of Cocoa, Helvetica Chimica Acta, 1975, Vol. 58, Iss. 4, 1975, pp. 1078-1086, discloses dipeptides that have been identified in roasted cocoa causing the typical bitterness.



Bonvehi, et al., Evaluation of Purine Alkaloids and Diketopiperazines Contents in Processed Cocoa Powder, Eur. Food Res. Technol., 2000, Vol. 210, pp. 189-195, discloses dipeptides obtained from cocoa powder that have a flavor.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer I. Harle whose telephone number is (571) 272-2763. The examiner can normally be reached on Monday through Thursday, 6:30 am to 5:00 pm,.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on (571) 272-0974. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



**MICHAEL MELLER**  
**PRIMARY EXAMINER**

Jennifer Ione Harle  
December 6, 2004

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